World Health Organization

World Health Organization: Update on AMR

Developing a fit for purpose response

Hanan H. Balkhy,
Assistant-Director General Antimicrobial Resistance, WHO
Geneva, Switzerland

Presidential Advisory Council on Combating Antibiotic-Resistant Bacteria (PACCARB)
Virtual Public Meeting, Nov 30, 2021

A major threat to global health

Drug-resistant infections are affecting the lives of thousands worldwide

Current and future impact of AMR

1 child dies every **3 min** from MDRO sepsis[1]

10 million AMR-related deaths by 2050[2]

28 million people living in poverty by 2050[3]

US$ 1 trillion additional healthcare Costs by 2050[3]

7.5% decline in livestock by 2050[3]

1. Ramanan Laxminarayan et al. Access to effective antimicrobials: a worldwide challenge. Lancet. 2016; 387: 168-175 / https://www.reactgroup.org/news-and-views/news-and-opinions/year-2020/new-react-film-children-at-risk-the-threat-of-antibiotic-resistance/; 2. Jim O' Neill (2016), Tackling Drug-Resistant Infections Globally: final report and recommendations, Review on Antimicrobial Resistance; 3. https://www.worldbank.org/en/topic/health/publication/drug-resistant-infections-a-threat-to-our-economic-future

World Health Organization

A One Health response to AMR

A sustained Global/National One Health Response is essential to tackle antimicrobial resistance and achieve the Sustainable Development Goals

Humans

Food & feed

Plants & crops

Environment

Terrestrial & aquatic animals

World Health Assembly & United Nations General Assembly

WHA68.7
2015[1]

UN-HLM on AMR
2016[2]

UNSDCF
2019[3]

UN call to action
2021[4]

WHO establishes the AMR Division
2019

1. https://www.who.int/publications/i/item/9789241509763; 2. https://cdn.who.int/media/docs/default-source/documents/no-time-to-wait-securing-the-future-from-drug-resistant-infections-en.pdf?sfvrsn=5b424d7_6&download=true, 3. https://unsdg.un.org/sites/default/files/2019-10/UN-Cooperation-Framework-Internal-Guidance-Final-June-2019_1.pdf; 4. https://www.un.org/pga/75/wp-content/uploads/sites/100/2021/04/Call-to-Action-on-Antimicrobial-Resistance-AMR-2021.pdf

World Health Organization

Antimicrobial Resistance Division

Leading, guiding and facilitating the Organization's global response to AMR, based on Global Action Plan on AMR, the 13th GPW and the SDGs

Strategic Priorities

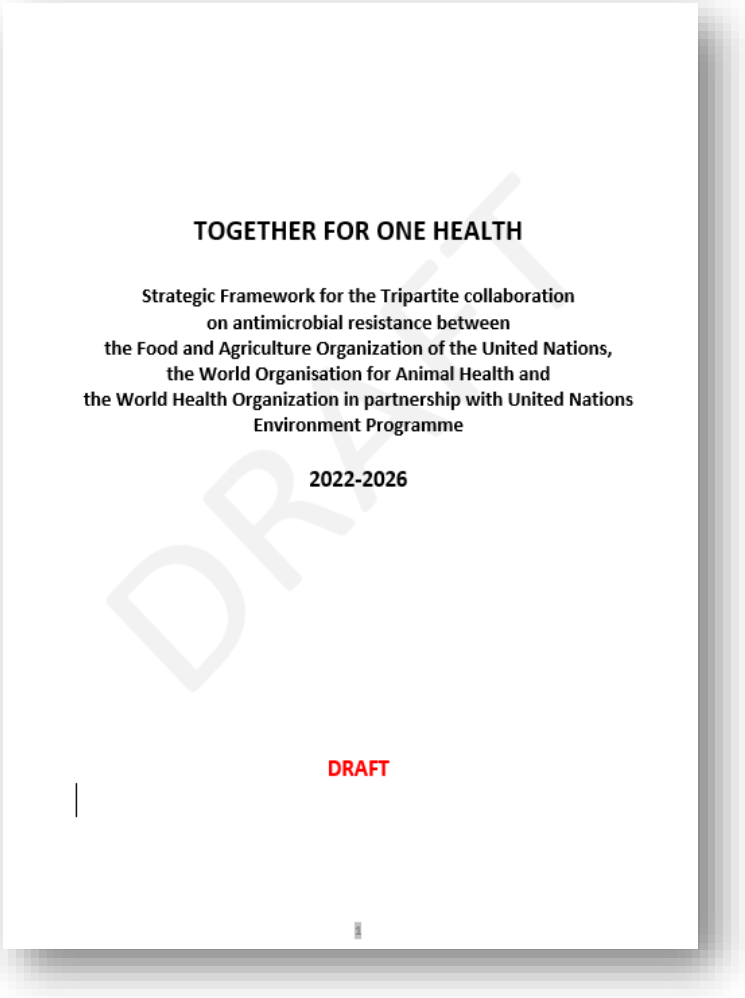
1. Stepping up leadership for the AMR response
2. Driving public health impact in every country
3. Research and development for better access to quality AMR prevention care
4. Monitoring the AMR burden and global AMR response

1. Stepping up leadership for the AMR response

Strategic Framework for the Tripartite Collaboration on AMR

Tripartite, UNEP and Partner coordination intensified for impact

- The Tripartite and UNEP are finalizing their Five Strategic Framework.
- The launch is expected to take place in early 2022.
- A two-year workplan, currently being developed, will accompany the framework.



Sustained political action is needed for the AMR response

Call to Action on Antimicrobial Resistance, High-Level Interactive Dialogue, UNGA, 29 April 2021

- 113 Member State signatories and 35 supporting organizations

Global Leaders Group has advisory and advocacy functions

FINANCING TO ADDRESS ANTIMICROBIAL RESISTANCE

Information note of the Global Leaders Group on Antimicrobial Resistance.
July 2021.

GLOBAL LEADERS GROUP ON ANTIMICROBIAL RESISTANCE

KEY MESSAGES

1. There is inadequate financial support currently available for the sustainable implementation of national action plans on antimicrobial resistance, particularly in low- and middle-income countries (LMICs). Increased investment is urgently needed to support countries to deliver on national action plans.
2. There is a strong economic case for investing in containment of antimicrobial resistance but robust estimates of the costs and benefits of implementing national action plans on antimicrobial resistance are needed to galvanize investment. The response to antimicrobial resistance also needs to be integrated into national pandemic preparedness and response plans.
3. Ongoing investment by governments, global/regional/national/bilateral/multilateral financing and development institutions and banks and private investors to build and bolster human health, animal health, food, plant and environmental eco-systems is crucial to tackling antimicrobial resistance and achieving sustainable development, with particular emphasis on infection prevention and control.
4. More financial support and incentives are needed for increased, effective and affordable innovations across all sectors and stakeholders (including the private sector) to secure a sustainable pipeline for new antimicrobials (particularly antibiotics), vaccines, diagnostics, waste management tools and safe and effective alternatives to antimicrobials, and to ensure equitable access to them.
5. The 2021 Call to Action on Antimicrobial Resistance commits signatories to work towards sufficient and sustainable funding for antimicrobial resistance-specific and antimicrobial resistance-sensitive actions across One Health, including as part of Covid-19 recovery plans and achieving universal health coverage, the Tripartite organizations and UNEP, and other relevant UN and multilateral organizations, including the Multi-Partner Trust Fund (MPTF) on AMR, as well as integration of antimicrobial resistance into the UN Financing for Development agenda.

1. The World Bank has made strikingly clear the economic case for investing in containment of antimicrobial resistance.

Investing in containment of antimicrobial resistance is considered to be a high-yield development investment with estimated returns far outweighing the costs. Without investment, the economic impacts of antimicrobial resistance are expected to lead to a rise in extreme poverty and a significant annual reduction in global GDP. In a high-impact antimicrobial resistance scenario, World Bank estimates suggest that the world stands to lose 3.8 percent of its annual GDP by 2050.[1]

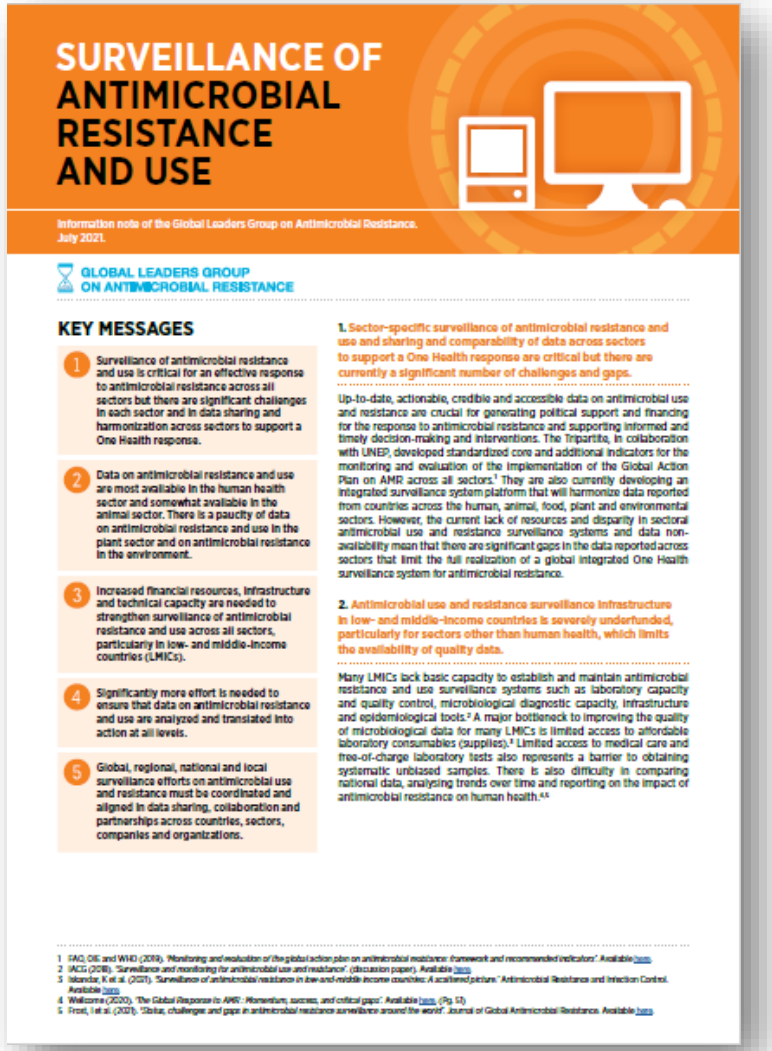
2. Robust estimates of the costs of implementing national action plans on antimicrobial resistance are needed to galvanize investment.

Existing estimates of the costs of antimicrobial resistance containment measures and national action plan implementation have been provided by the O'Neill Review on Antimicrobial Resistance in 2016 and the World Bank in 2017. These estimates range from US $4-9 billion annually,[2,3] but experts have suggested that these figures may considerably underestimate the true cost of responding to antimicrobial resistance in a One Health context. By comparison, in 2020 there was an estimated need of US $26 billion and US $15 billion to respond to HIV and TB respectively, of which almost US $20 billion (in 2019 for HIV) and nearly US $7 billion (in 2020 for TB) was available.[4,5] More robust cost and benefit estimates are needed to galvanize investment in the response to antimicrobial resistance.

3. Antimicrobial resistance is currently not a financing priority for many LMICs.

For many countries, the benefits of containing antimicrobial resistance may not be perceived as immediate or tangible compared to other development priorities. COVID-19 fiscal constraints may also lead to a reduction in the financing of antimicrobial resistance programmes across sectors in coming years.[6] Incorporating antimicrobial resistance

1 World Bank (2017). 'Drug-Resistant Infections: A Threat to Our Economic Future.' Available here. (Pgs. xx, xviii and 32)
2 World Bank (2017). 'Drug-Resistant Infections: A Threat to Our Economic Future.' Available here. (Pg. xx)
3 The Review on Antimicrobial Resistance (2016). 'Tackling drug-resistant infection globally: Final report and recommendations.' Available here. (Pg. 7)
4 UNAIDS (2021). 'End Inequalities. End AIDS. Global AIDS Strategy 2021-2026'. Available here. (Pg. 38).
5 WHO (2020). 'Global Tuberculosis Report 2020'. Available here. (Pg. 129)
6 Wellcome (2020). 'The Global Response to AMR: Momentum, success, and critical gaps'. Available here. (Pgs. 15 and 42)



SURVEILLANCE OF ANTIMICROBIAL RESISTANCE AND USE

Information note of the Global Leaders Group on Antimicrobial Resistance.
July 2021.

GLOBAL LEADERS GROUP ON ANTIMICROBIAL RESISTANCE

KEY MESSAGES

1. Surveillance of antimicrobial resistance and use is critical for an effective response to antimicrobial resistance across all sectors but there are significant challenges in each sector and in data sharing and harmonization across sectors to support a One Health response.
2. Data on antimicrobial resistance and use are most available in the human health sector and somewhat available in the animal sector. There is a paucity of data on antimicrobial resistance and use in the plant sector and on antimicrobial resistance in the environment.
3. Increased financial resources, infrastructure and technical capacity are needed to strengthen surveillance of antimicrobial resistance and use across all sectors, particularly in low- and middle-income countries (LMICs).
4. Significantly more effort is needed to ensure that data on antimicrobial resistance and use are analyzed and translated into action at all levels.
5. Global, regional, national and local surveillance efforts on antimicrobial use and resistance must be coordinated and aligned in data sharing, collaboration and partnerships across countries, sectors, companies and organizations.

1. Sector-specific surveillance of antimicrobial resistance and use and sharing and comparability of data across sectors to support a One Health response are critical but there are currently a significant number of challenges and gaps.

Up-to-date, actionable, credible and accessible data on antimicrobial use and resistance are crucial for generating political support and financing for the response to antimicrobial resistance and supporting informed and timely decision-making and interventions. The Tripartite, in collaboration with UNEP, developed standardized core and additional indicators for the monitoring and evaluation of the implementation of the Global Action Plan on AMR across all sectors.[1] They are also currently developing an integrated surveillance system platform that will harmonize data reported from countries across the human, animal, food, plant and environmental sectors. However, the current lack of resources and disparity in sectoral antimicrobial use and resistance surveillance systems and data non-availability mean that there are significant gaps in the data reported across sectors that limit the full realization of a global integrated One Health surveillance system for antimicrobial resistance.

2. Antimicrobial use and resistance surveillance infrastructure in low- and middle-income countries is severely underfunded, particularly for sectors other than human health, which limits the availability of quality data.

Many LMICs lack basic capacity to establish and maintain antimicrobial resistance and use surveillance systems such as laboratory capacity and quality control, microbiological diagnostic capacity, infrastructure and epidemiological tools.[2] A major bottleneck to improving the quality of microbiological data for many LMICs is limited access to affordable laboratory consumables (supplies).[3] Limited access to medical care and free-of-charge laboratory tests also represents a barrier to obtaining systematic unbiased samples. There is also difficulty in comparing national data, analysing trends over time and reporting on the impact of antimicrobial resistance on human health.[4,5]

1 FAO, OIE and WHO (2018). 'Monitoring and evaluation of the global action plan on antimicrobial resistance: framework and recommended indicators'. Available here.
2 IACG (2018). 'Surveillance and monitoring for antimicrobial use and resistance'. (discussion paper). Available here.
3 Iskandar, K et al. (2021). 'Surveillance of antimicrobial resistance in low-and-middle income countries: A scattered picture.' Antimicrobial Resistance and Infection Control. Available here.
4 Wellcome (2020). 'The Global Response to AMR: Momentum, success, and critical gaps'. Available here. (Pg. 13)
5 Frost, I et al. (2021). 'Status, challenges and gaps in antimicrobial resistance surveillance around the world'. Journal of Global Antimicrobial Resistance. Available here.

ANTIMICROBIAL RESISTANCE AND THE CLIMATE CRISIS

Information note of the Global Leaders Group on Antimicrobial Resistance.
October 2021.

GLOBAL LEADERS GROUP ON ANTIMICROBIAL RESISTANCE

KEY MESSAGES

1. The climate crisis and antimicrobial resistance - the ability of microbes to resist the drugs designed to inhibit or kill them - are two of the greatest and most complex threats currently facing the world. Both have been exacerbated by, and can be mitigated with, human action.
2. The climate crisis is impacting human health, animal health, food, plant and environment eco-systems in numerous ways, and many of these impacts could affect antimicrobial resistance.
3. Evidence suggests that changes occurring in the natural environment due to the climate crisis are increasing the spread of infectious disease, including drug-resistant infections.
4. High usage of antimicrobial drugs across sectors exacerbates antimicrobial resistance. The increasingly severe impacts of the climate crisis, such as more frequent and severe extreme weather events, will likely result in an increased use of antimicrobial drugs in humans, animals and plants.
5. As these two crises continue to grow, the impacts on economies, lives, and livelihoods are expected to be significant and devastating, particularly for low-and middle-income countries and small island developing states.
6. More financing, political advocacy and coordinated global action are needed to better understand and respond to the converging threats of antimicrobial resistance and the climate crisis before it is too late.
7. The links between antimicrobial resistance and the climate crisis have been neglected and require significantly more attention, including in national action plans on antimicrobial resistance. There is currently no global initiative focused specifically on the intersection of these two crises.

1. The climate crisis[1] is already affecting patterns of infectious disease and worsening existing health challenges, which may lead to an increase in the use of antimicrobial drugs and antimicrobial resistance.

Many diseases are climate-sensitive and changes in environmental conditions and temperatures may lead to an increase in the spread of many bacterial, viral, parasitic, fungal, and vector-borne diseases in humans, animals and plants. Increased prevalence of disease could result in an increase in the improper use of antimicrobial drugs, which could exacerbate antimicrobial resistance. For example, the climate crisis is a key driver of changes in the spread and distribution of helminths (parasitic worms which can cause severe illness and death in humans and animals) in livestock, with large-scale outbreaks of helminths becoming increasingly common.[2] The climate crisis is also affecting human and animal habitats and ranges, which may increase the risk of human exposure to some vector-borne diseases.[3] In Europe, for example, sand flies (which can transmit the disease leishmaniasis) are at present mainly found in the Mediterranean region, but with the climate crisis sand fly species are expected to expand their range into central and northern Europe.[4]

In 2019, nearly half of the world's population was at risk of malaria.[5] Climatic changes, such as more extreme weather events which bring increased rainfall, temperature and humidity may also increase the incidence of malaria in areas where it is already present and lead to it spreading into new areas.[6] As drug resistance for some vector-borne diseases is increasing, climate crisis-associated diseases such as malaria may become harder to contain and treat because the antimicrobial medicines relied on for treatment are becoming less effective. Malaria parasites have already demonstrated resistance to almost every antimalarial drug currently available.[7]

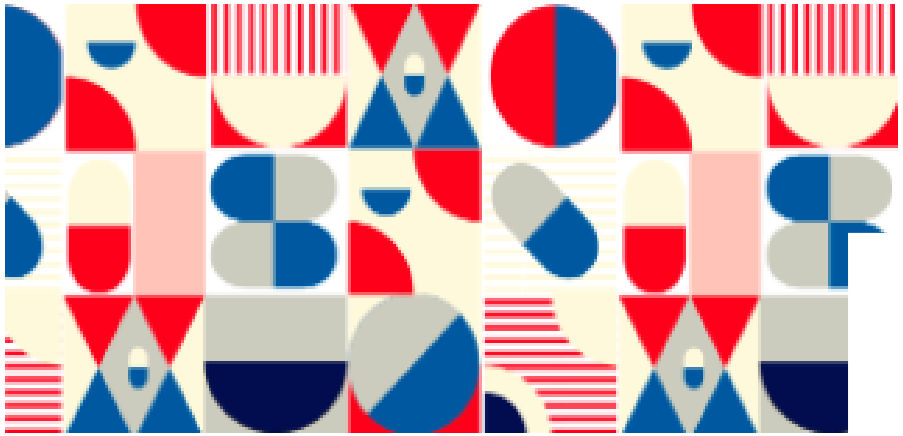
1 The term 'climate crisis' refers to global warming and climate change. Climate change refers to changes that alter the global atmosphere composition and are directly or indirectly attributed to human activity (UNFCCC (1992). Available here.) The effects of this include increases in global temperatures and in the frequency and intensity of extreme weather events (IPCC (2018). Available here.)
2 Fox, N et al. (2015). 'Climate-driven tipping-points could lead to sudden, high-intensity parasite outbreaks'. Royal Society Open Science. Available here.
3 Gonzalez, C et al. (2010). 'Climate Change and Risk of Leishmaniasis in North America: Predictions from Ecological Niche Models of Vector and Reservoir Species'. Plos Neglected Tropical Diseases. Available here.
4 Koch, L et al. (2017). 'Modeling the climatic suitability of leishmaniasis vector species in Europe'. Nature Scientific Reports. Available here.
5 WHO. 'Malaria'. [webpage]. Available here. (Accessed 24 September 2021)
6 Fernando, S. 'Climate change and malaria: A complex relationship'. UN Chronicle. Available here.
7 WHO (2001). 'Drug Resistance in Malaria'. Available here.

World Health Organization

The Partnership Platform for AMR is in the making

Bringing civil society, government and private sector together for a shared vision

AMR Multi-Stakeholder Partnership Platform - Creating a movement for change through engaging multiple actors and voices



18/08/2021

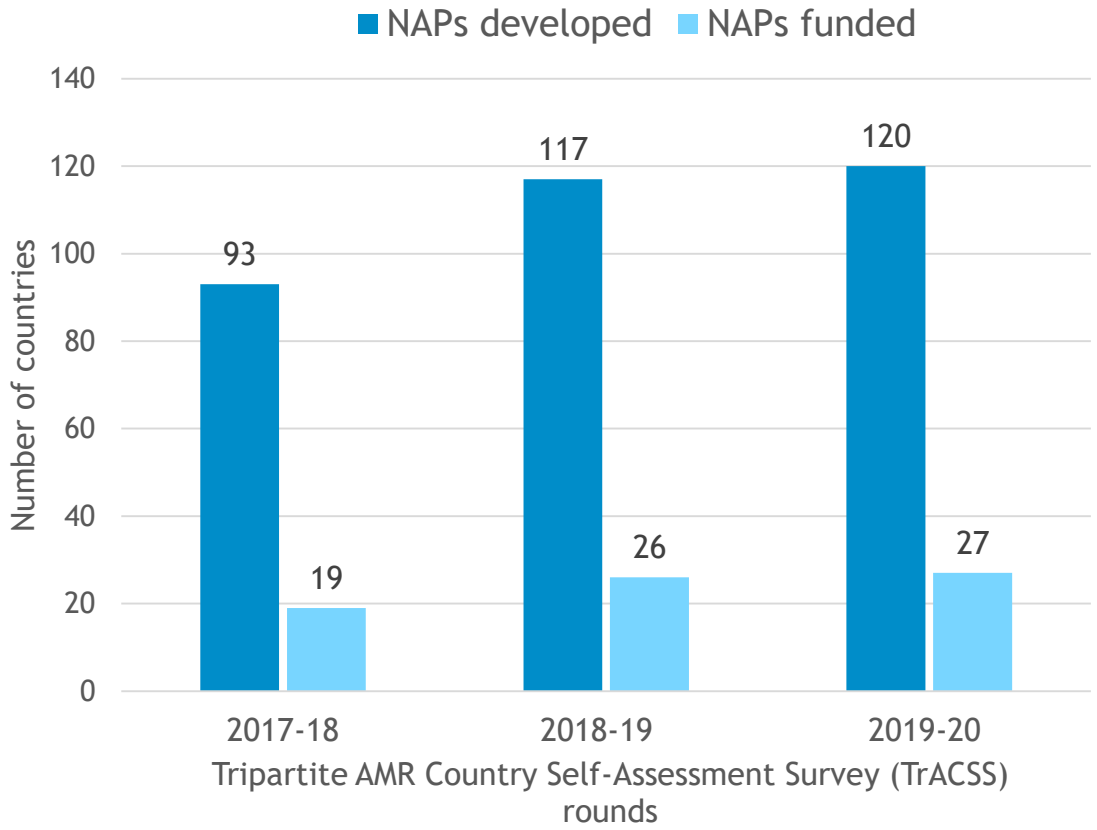
The Tripartite organizations (FAO, OIE, WHO) invite partners to join public discussion on the establishment of the AMR Multi-Stakeholder Partnership Platform

2. Driving public health impact in every country

Acceleration of National Action Plan Implementation

163 responding countries have developed multisectoral AMR national action plans, but only 20% of the countries are actively monitoring their implementation and have allocated funding (2021 TrACSS data)

- WHO through the 3 levels of the Organization – Headquarters, Regional Offices and Country Offices – and Partners
- Scaling up support for country implementation of AMR national action plans
- Working closely with all other sectors to address AMR through a One Health approach
- Critical for achieving the 2030 Agenda for Sustainable Development
- Essential to integrate AMR in achieving UHC, strengthen health systems, and build capacity to address future pandemic prevention and preparedness.



World Health Organization

WHO NAP Implementation Handbook

February 2022

- Describes a practical 6 step process at country level:
  1. Strengthen governance / coordination
  2. Prioritize activities
  3. Cost the operational plan
  4. Mobilize resources
  5. Implement prioritized activities
  6. Monitor and evaluate

- Collation of new and existing WHO tools and guidance to support each step (a living document)

who.int/media/docs/default-source/antimicrobial-resistance/amr-spc-npm/nap-support-tools/amr-resource-pack-2021.pdf?sfvrsn=72141940_7

World Health Organization

3. Research and development for better access to quality AMR prevention care

R&D Priority Setting and Coordination

Priority setting & coordination

- Priority Pathogens List update 2022
- Fungal Priority Pathogens 2022
- Antibiotic, fungal and vaccine pipeline
- One Health research agenda

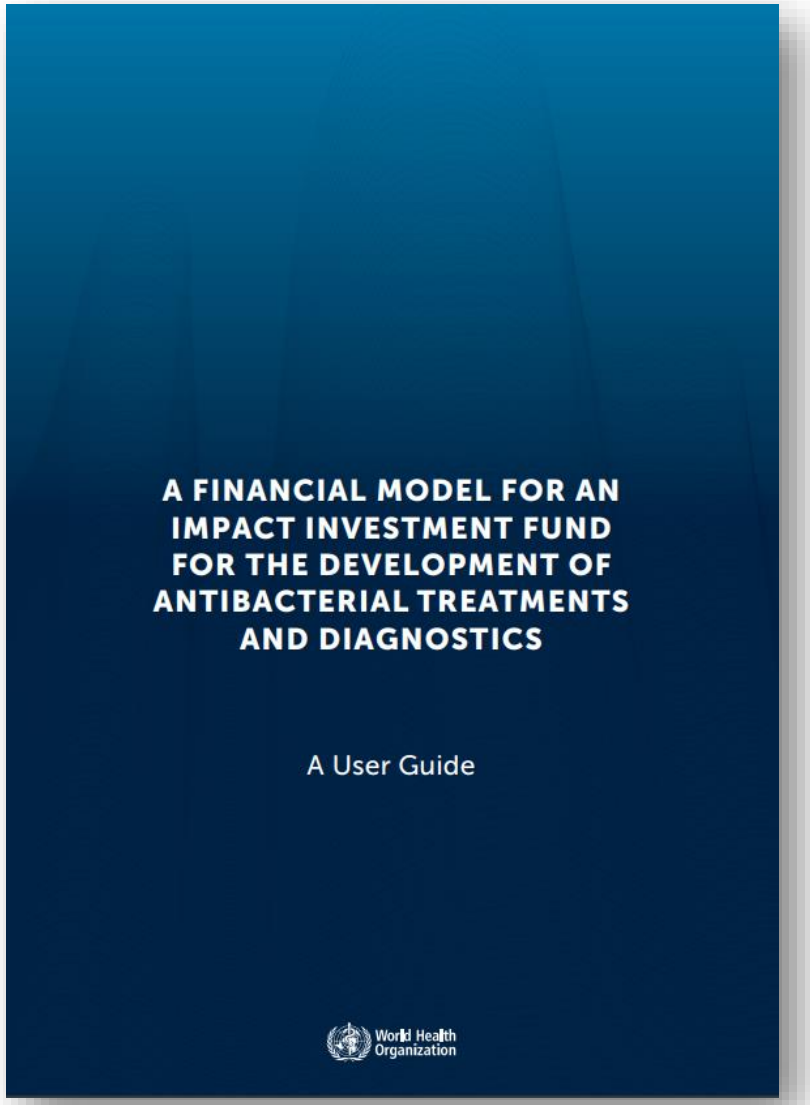
Fostering R&D

- GARDP
- AMR Action Fund

Fostering access

- SECURE

AMR Action Fund launched in July 2020



AMR Action Fund driven by pharmaceutical industry:

- **USD1BN investment** by pharmaceutical companies and EIB
- Invests into innovative antibacterial agents that target public health priorities
- Focus on clinical phases II and III
- WHO involved in the set up and to guide public health priorities and access and appropriate use strategies
- WHO developed financial model that estimates the potential returns on investments into the fund given the information available on R&D costs and progression rate through development phases
- https://www.who.int/publications/i/item/a-financial-model-for-an-impact-investment-fund-for-the-development-of-antibacterial-treatments-and-diagnostics-a-user-guide
- https://amractionfund.com/

Antimicrobial R&D, access and research priority setting

secure

Expanding Sustainable Access to Antibiotics

World Health Organization · GARDP · Clinton Health Access Initiative · unicef for every child

The antibiotic facility

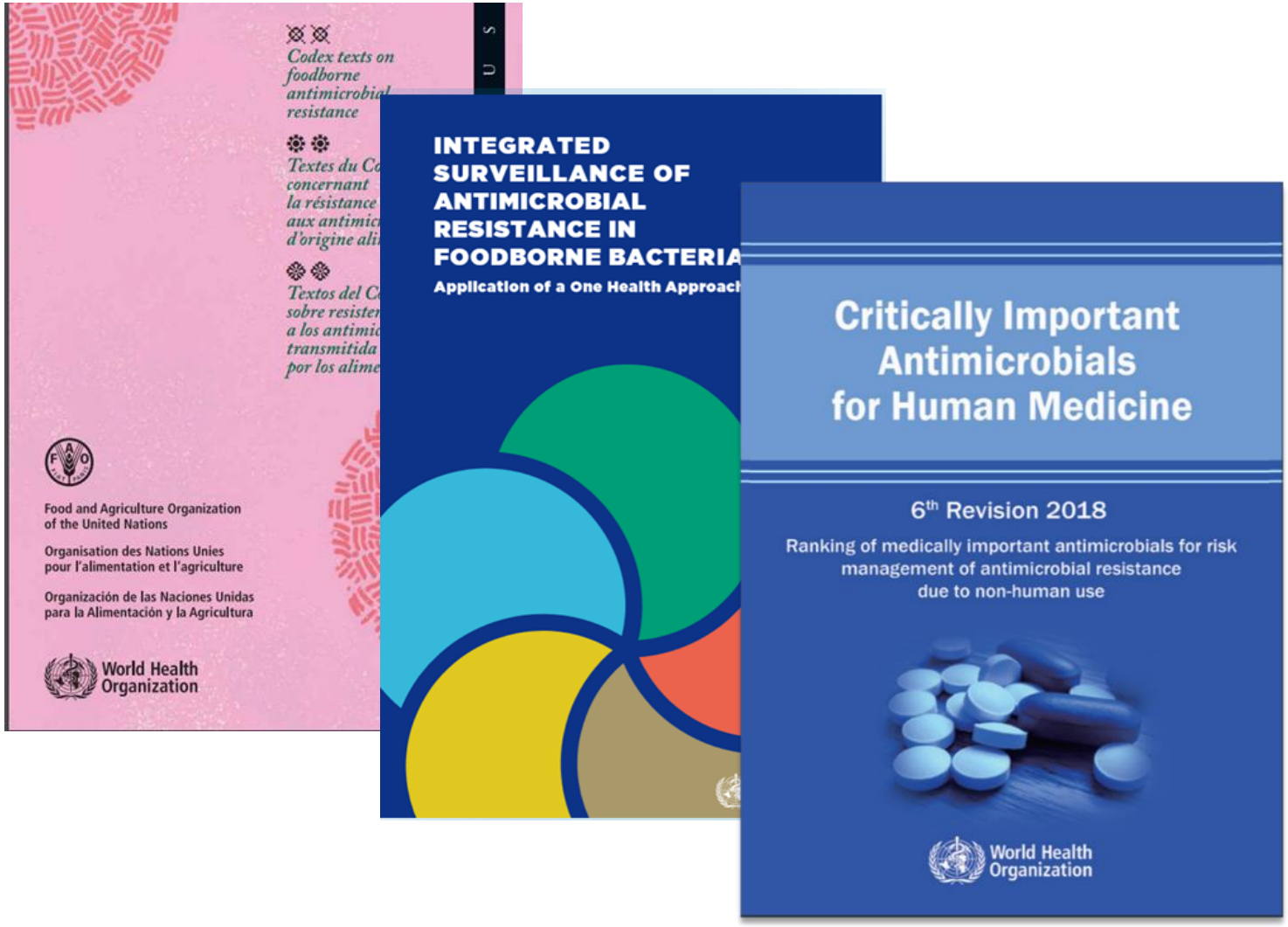
SECURE will **provide countries with sustainable access to:**

(1) **new antibiotics** to address drug-resistant infections
(2) **existing antibiotics** that are not widely available or that suffer from frequent supply chain interruptions and/or shortages

- SECURE will establish a quality assured portfolio **driven by public health and clinical needs** and
- **Open to all interested countries and other eligible entities**
- **Included in ongoing G7 discussions**

Codex Alimentarius to address food borne antimicrobial resistance & Antimicrobial stewardship across One Health sectors

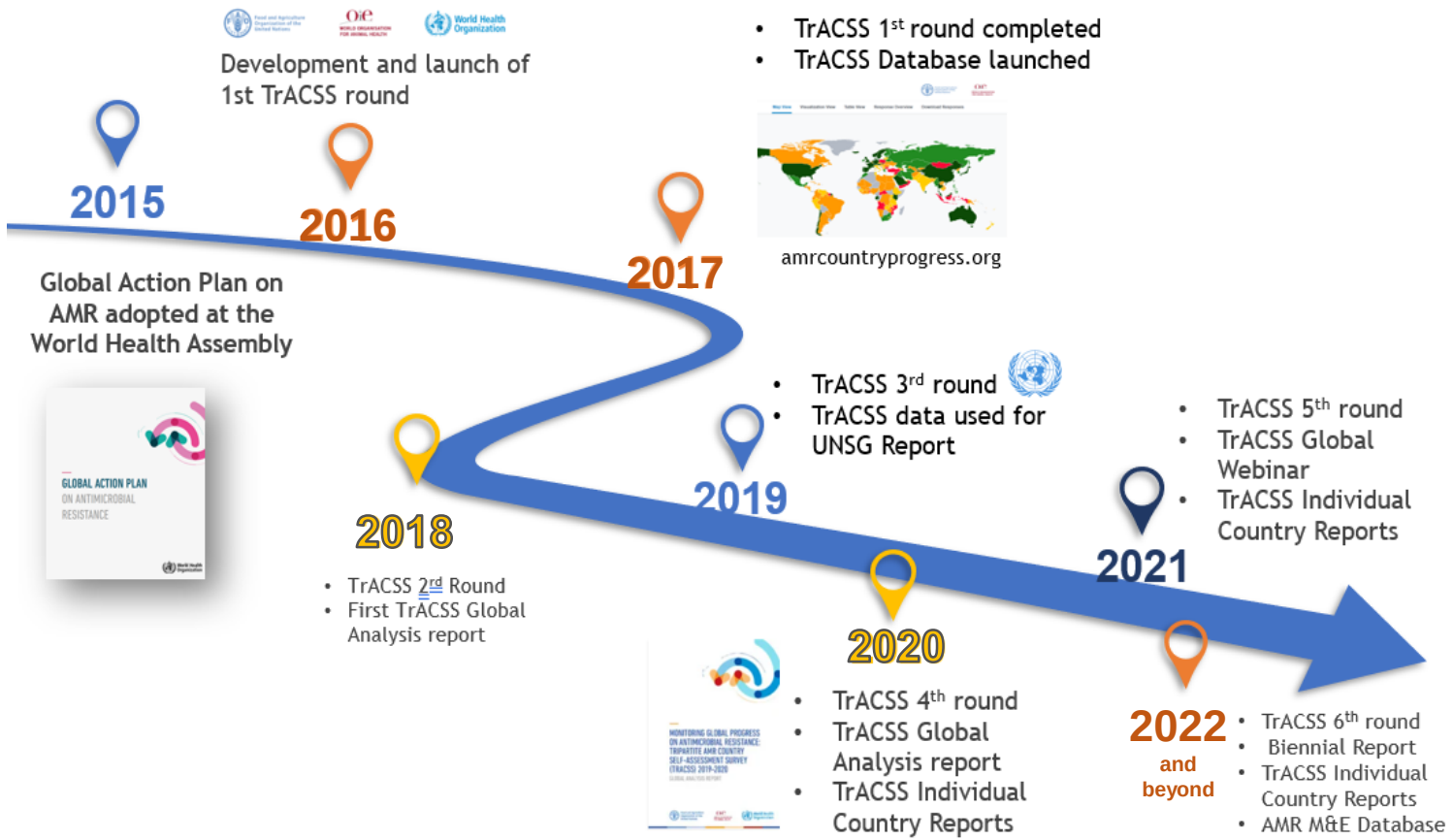
- Review and revise Code of Practice to Minimize and Contain Antimicrobial Resistance
- Codex Guidelines on Integrated Surveillance of Antimicrobial Resistance (GLIS)
- **CIA List – 7 Revision 2021.** Ranking of medically important antimicrobials for risk management of antimicrobial resistance due to non-human use.



4. Monitoring the AMR burden and global AMR response

2021 Tripartite AMR Country Self-Assessment Survey (TrACSS)

An annual survey monitors the implementation of AMR NAPs since 2016



TrACSS is based on the AMR GAP and monitors country implementation of AMR national action plans

Survey includes indicators on:

- NAPs and governance
- Education and awareness
- IPC, WASH and immunization
- Antimicrobial resistance and consumption surveillance; labs
- Optimize use and AWaRe
- Environment, and links to other diseases

SDG Indicator - Proportion of bloodstream infections

E. coli resistant to 3rd generation cephalosporins, MRSA and Acinetobacter resistant to carbapenems

SDG indicators/GLASS

E. coli

resistant to 3rd generation cephalosporins

Global median 37%

Interquartile range (IQR) of 17-58%, reported by 60 countries in 2019.

MRSA

Resistant to methicillin

Global median 25%

Interquartile range (IQR) of 11-40%, reported by 54 countries in 2019

GLASS

Acinetobacter

Resistant to carbapenems

Global median 64%

Interquartile range (IQR) of 18-78% (for Meropenem), reported by 57 countries in 2019

Footnote: These findings require further investigation to verify the reliability of the results and understand the reasons behind the differences in rates

Global Antimicrobial Resistance and Use Surveillance System (GLASS) (who.int); https://unstats.un.org/sdgs/unsdg

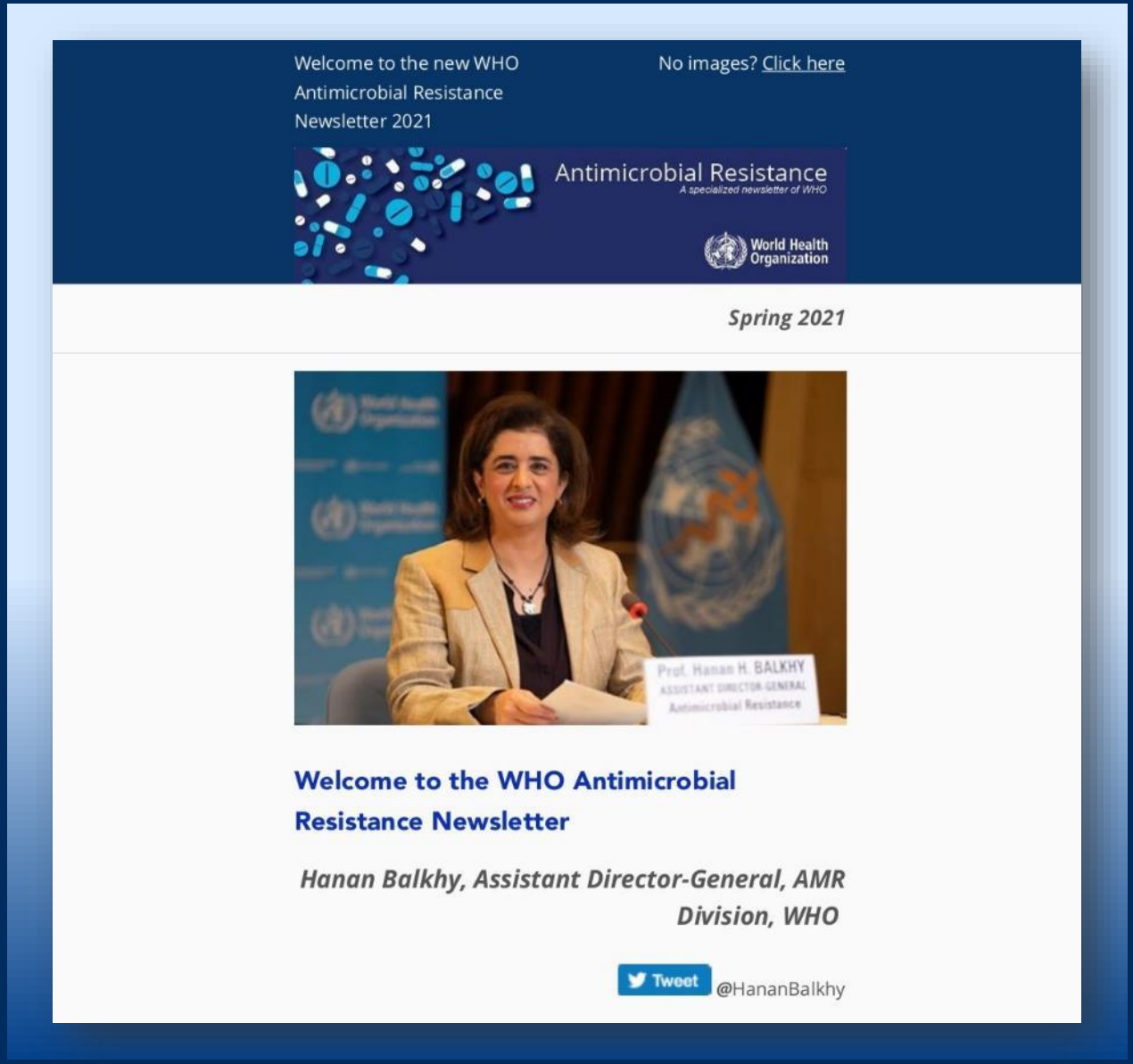
World Health Organization

WHO response: generate data that can and will be used

National AMR surveys	• Representative comparable country data • Focus on SDG indicators to start with
Improve routine surveillance	• Quality criteria, progressive pathway, audits • TA : diagnostic stewardship, lab network, SCM
Guidance on use of data	• AMR/AMU/AMC data usability and practical use • Communication and translation into policies

Thank you

[WHO AMR Newsletter]



World Health Organization